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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,533	RAI ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28* is/are pending in the application.

4a) Of the above claim(s) *28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on February 14, 2008 is acknowledged. The traversal is on the ground(s) that the examination of group I and II do not pose an undue search burden.

This is not found persuasive because the groups have different special technical features. The process for a preparation can be used with methods or products. For instance, the kit has additional regents and components not required by group I. Specifically, the kit of group II requires storage buffer, glass slides, droppers, wooden stick and positive and negative controls. Therefore, the kit's special technical feature is comprised within the kit and not within the methods steps; therefore the groups lack the same or corresponding technical feature.

Applicants' argue that there would be no serious burden on the Examiner to search for the other groups. However, in the instant case these inventions are unrelated and distinct. The method is distinct as claimed because they are drawn to measuring or performing different activities. Furthermore the distinct steps and components of the kit require separate and distinct searches. The groups have a separate status in the art as shown by their different classification. As such, it would be burdensome to search the inventions of groups together. Furthermore, a search for the invention of the groups would not be coextensive because a search indicating the process of group I is novel or unobvious would not extend to a holding that the kit of group II is novel or unobvious. The process of preparation does not require glass slides,

droppers, wooden sticks and positive and negative controls. Because of the different classifications of each group based upon the distinct method steps, a serious burden is imposed on the examiner to perform a complete search of the defined areas in both the patent and non-patent literature. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden on the examination of this application.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The use of the trademark TRITON X-100™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

3. Claims 23 and 26 are objected to because of the following informalities:

a) Claim 23(i) recites “morphilinoethane” instead of “morpholinoethane”.

b) Claim 23(ii) recites “carbodimide” instead of “carbodiimide”.

c) Claim 26 recites “thiomersal” instead of “thimerosal”.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. Claims 23-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Regarding claim 23(i), the phrase "like rabbit" renders the claim indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

(b) Claims 23 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim scope is uncertain since the trademark or trade name TRITON X-100™ cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name TRITON X-100™ is used to identify/describe a particular material, i.e. a nonionic surfactant and accordingly, the identification is indefinite. Furthermore, the use of trademarks is improper since products identified by trademarks are within the sole control of the trademark owner and are subject to change by said owner at their discretion.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Lim et al., (J. Clinical Microbio. 1987. Vol. 25(7): 1165-1168).

Claim 24 is drawn to an agglutination reagent for rapid and early detection of typhoid, comprising of 1% carboxylated latex particles coated with antibody specific to *Salmonella typhi*, suspended in storage buffer. Claim 25 is drawn to the size of the said latex particles is 0.88 to 0.90 um. Claim 26 is drawn the storage buffer is comprised of 50 mM glycine pH 8.5, 1.0% bovine serum albumin, 0.03 % TRITON X-100^{TM}, 0.1% sodium azide and 0.01% thimerosal.

Lim et al., teach latex particles coated with a monoclonal antibody specific for *Salmonella typhi* (abstract). Lim et al., teach a 1% suspension of latex particles (page 1165, col.2). Lim et al., teach the latex antibody particles were washed in a glycine containing buffer containing 1.0% bovine serum albumin and 0.02 sodium azide. The carboxylated latex beads are commercial available from Sigma (page 1165, col.2). Lim et al, teach the coated beads suspended in storage buffer (page 1166, col. 1).

Therefore Lim et al., teach the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson et al., (Electrophoresis. 2001. Vol. 22:2384-2390) and Salzman et al (WO 01/40280 published June 1, 2001) in view of Sukosol et al., (Asian Pacific J. of Allergy and Immuno. 1994. Vol. 12. pages 21-25).

Claim 23 is drawn to a process for the preparation of an agglutination reagent for rapid and early detection of typhoid comprising: (a) preparing antibody specific to *Salmonella typhi*; (b) preparing latex particles suspension; (c) coating of the said latex particles with the said antibody; wherein the said process of preparing antibody specific to Salmonella typhi comprises cloning Flagellin gene sequence specific to *Salmonella typhi*, expressing the said Flagellin gene sequence by recombinant DNA technology, followed by purifying recombinant protein by affinity chromatography, raising the hyper immune sera against purified recombinant protein in animals like rabbit, separating the antibody (immunoglobulin) fraction of hyper immune sera by precipitating in ammonium sulphate, suspending in 50 mM phosphate buffer of pH 7.2 and dialyzing; wherein the said process of preparing latex particle suspension comprises:

(i) mixing 1% carboxylated latex particles of size 0.88 to 0.90 um and 40 mM 2-N Morpholinoethane sulphonic acid (MES) buffet of pH 5.5 to 6.0 in a ratio of 1:1 on a

vortex mixer for about 60 seconds, centrifuging at 10,000 rpm for 10-12 minutes at about 4°C, followed by washing twice with 20 mM MES buffer of pH 5.5 at 10,000 rpm for 10-12 minutes at about 4°C, sonicating by a tip sonicator at about 5 watts for 60-120 seconds; (ii) adding drop wise a freshly prepared solution of 0.1 M 1-ethyl-3 (3-dimethyl-amino propyl) carbodiimide hydrochloride (EDC) in 20 mM MES buffer of pH 5.5 to the said sonicated latex particles obtained from step (i) above in a ratio of 1:1 while vortexing the suspension slowly, rotating the suspension slowly end-over-end for about 3 hours at a temperature of 20-25°C washing thrice with 20 mM MES buffer (pH 5.5) followed by sonicating the washed suspension of latex particles by a tip sonicator for 60-120 seconds at about 5 watts; wherein the said process of coating of the said latex particles is done by adding 0.6-1.0 mg preferably 0.8 mg per ml of the said antibody (immunoglobulins) to the said latex particle suspension, rotating the suspension end-over-end for 18-20 hours at a temperature of about 20-25°C, stopping the coating reaction by 1M glycine (pH 11.0) taken in quantity of 0.06 ml per ml of solution of antibody coated latex particles followed by centrifugation at 10,000 rpm for 10-12 minutes at a temperature of about 4°C, washing thrice with washing buffer comprised of 50 mM glycine, pH 8.5; 0.03% TRITON X-100™ and 0.05% sodium azide, suspending in storage buffer to a final concentration of 1%, sonicating for about 60 seconds at about 5 watts and storing at 4°C.

Claim 24 is drawn to an agglutination reagent for rapid and early detection of typhoid, comprising of 1% carboxylated latex particles coated with antibody specific to *Salmonella typhi*, suspended in storage buffer. Claim 25 is drawn to the size of the said

latex particles is 0.88 to 0.90 um. Claim 26 is drawn the storage buffer is comprised of 50 mM glycine pH 8.5, 1.0% bovine serum albumin, 0.03 % TRITON X-100™, 0.1% sodium azide and 0.01% thimerosal. Claim 27 is drawn wherein the antibody is the immunoglobulin fraction, of the hyper immune sera raised in rabbit against the recombinant protein expressed by cloning of Flagellin gene sequence specific to *Salmonella typhi* by recombinant DNA technology, suspended in 50 mM phosphate buffer.

Nilsson et al., teach a general method applicable to most proteins that creates a system for highly selective and sensitive protein detection (page 2384, col.1). Nilsson et al., teach antibodies-coated particles used in agglutination assays give more rise to limits of detection in the lower attomole regions of fully optimized systems (page 2384, col.2). Nilsson et al., teach the materials to include: affinity purified antibodies, carboxylated latex particles, 2-(N-Morpholino)ethane0sulfonic acid (MES), ethyl-3(3-dimethylaminopropyl)-carbodiimide (EDC). Bovine serum albumin (BSA),TWEEN 20, Tris, sodium hydroxide, and other reagents (page 2385, col1). Nilsson et al., teach covalent coupling of antibodies to latex particles (page 2385, col.1). The carboxylated latex particles (0.9um) were washed by centrifugation (14, 000xg, 10 minutes) in MES buffer, pH 5.5 and resuspended (page 2385, col1). EDC was added to the particles, and the mixture was incubated under vortexing (page 2385. col. 1). Nilsson et al., antibody solution containing BSA was added to the activated particles. Coupling protein with vortexing on ice, followed by incubation. Nilsson et al., teach activated carboxyl groups were then blocked by adding Tris-HCl; sonicating the particles and washing four

times by centrifugation with Tris-BSA buffer (page 2385, col. 1-2). For fluorescent carboxylated latex particle, during activation MES buffer, pH 5.5 containing Tween 20 was used to prevent particle aggregation (page 2385, col. 2). Nilsson et al., teach the use 1% of carboxylated latex particles suspended in Tris-BSA buffer (page 2385, col. 2). However Nilsson et al., do not teach preparing an antibody specific to *Salmonella typhi* comprising cloning the Flagellin gene.

Salzman et al., teach obtaining flagellin peptides from Salmonella species wherein the flagellin polypeptide (page 4, para. 3). Salzman et al., teach the flagellin polypeptide or a flagellin fusion polypeptide can be synthesized using standard art recognized recombinant DNA techniques (page 8, para. 3). Salzman et al., teach obtaining purified flagellin that is free from cellular material or other contaminating proteins (page 6, para. 2). Example 1 teaches using affinity purification techniques to purify the recombinantly produced flagellin. Salzman et al, also teach antibodies to the flagellin polypeptides (page 10, para. 3). Salzman et al., teach the production of polyclonal antibodies with immunization in a host animal such as a rabbit, wherein one of more injections of the synthetic (recombinant) protein are administered (page 12, para. 3). Salzman et al., teach the polyclonal antibodies are isolated by well known techniques including ammonium sulphate precipitation (page 13, para. 1). Salzman et al, also teach monoclonal antibody purification by conventional immunoglobulin purification procedures including dialysis techniques (page 14, para. 4). However Salzman et al., do not teach recombinant fusion protein of flagellin protein from *Salmonella typhi.*

Sukosol et al., teach the production of recombinant fusion protein of flagellin protein from *Salmonella typhi* (page 21, col. 1). Sukosol et al., teach that the antibodies do not cross react with relation proteins from 11 other bacteria causing enteric fever and enteric fever-like illness (page 21, col.1-2). Sukosol et al., teach the construction and screened for the recombinant clones expressing specific *S. typhi* antigens (page 21, col.3). The gene was the flagellin gene and the flagellin DNA was amplified using PCR technology (page 22, col.1-3).

Therefore it would have been prima facie obvious at the time of applicants' invention to apply the antibody specific to *Salmonella typhi* as taught by Sukosol et al., and the preparation of the antibody as taught by Salzman et al., to the method for the preparation of latex particles as taught by Nilsson et al., in order to provide improve the detectability. One of ordinary skill in the art would have a reasonable expectation of success by exchanging the flagellin *Salmonella* typhi antibody with other *Salmonella* flagellin antibodies because are they are known to be recombinantly prepared and capable of being coated onto latex particles in order to provide specific binding. Furthermore, no more than routine skill would have been required to exchange the antibody of Salzman et al., for the well known and functionally equivalent antibody Sukosol et al., since discloses the benefits of antibodies that specifically bind to flagellin. Finally it would have been prima facie obvious to combine the invention of Salzman, Sukosol and Nilsson et al., to advantageously achieve a general method applicable to most proteins that creates a system for highly selective and sensitive protein detection.

Conclusion

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Shanon Foley, can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/

Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645